REMARKS

Reconsideration of the rejections set forth in the Office Action mailed January 12, 2005, is respectfully requested. Claims 25-27 and 33-36 have been canceled. Claims 1-11 remain pending.

Amendments to the Specification

Applicants discovered a typographical error in the chemical structure of dalbavancin on page 11 -- the connectivity of one of the bonds to a phenyl ring is misplaced. The correct structure of dalbavancin is well known and is set forth elsewhere in the present application. As published in U.S. Patent No. 5,750,509 (Attached as Exhibit A, see formula (I) in Col. 1), incorporated by reference in the present application at paragraphs 0039 and 0255, the connectivity to the phenyl ring at position (15) of the carbon is *para* to the OH substituent, not *meta*. Therefore, applicants respectfully request correction of this structure.

Preliminary Amendment

Applicants would first like to point out to the examiner that claims 12-24, 28-32, and 37-66 were previously canceled in the preliminary amendment filed on April 16, 2004. Applicants have additionally canceled 25-27 and 33-36 with this amendment. Claims 1-11 remain pending.

Double Patenting

Claims 12-24, 28-32, 37-43, and 54-66 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 57-78 of co-pending Application Serial No. 10/714,261, claims 1-23 of co-pending

Application Serial No. 10/828,379, and claims 1-45 of co-pending Application Serial No. 10/828,483.

Applicants have canceled claims 12-24, 28-32, 37-43, and 54-66. Therefore, these rejections are now moot. Therefore, applicants respectfully request withdrawal of these double patenting rejections.

Art Rejections

Claims 1-66 were rejected under 35 U.S.C. § 103(a) as being allegedly anticipated by "Dalbavancin Tested for Soft Tissue Infections " (2001) or "Molecule of the Month V-Glycopeptide" submitted in view of Tucker et al. (U.S. Patent No. 6,541,616). The examiner has taken the position that although the cited references do not disclose dalbavancin in combination with a stabilizer, a person having ordinary skill in the art would have been motivated to combine dalbavancin with a conventional stabilizer because the results from such a combination would have been expected.

Claims 12-66 have been canceled. Therefore, the rejections to these claims are now moot.

With respect to claims 1-11, applicants respectfully submit that one skilled in the art would not be motivated to combine the teachings of "Dalbavancin Tested for Soft Tissue Infections " (2001) or "Molecule of the Month V-Glycopeptide" with the teachings of Tucker et al. Tucker et al. is in an unrelated field, namely isolating proteins and producing vaccines for use against *M. catarrhalis* infections. (See Col. 3, lines 54-57, "An object of the present invention is to provide an isolated or substantially purified OMP21 protein of a *M. catarrhalis* strain, wherein the apparent molecular weight is about 16 kD to about 20 kD.") Section 5.5 of the '616 patent

describes pharmaceutical compositions, namely vaccines, that can be used treat *M. catarrhalis* infections in animals. (See Col. 18, lines 32-38, "More preferred immunogeneic compositions, including vaccines are cocktail vaccines that comprise OMP21 in combination with OMP106 and one or more adjuvants.")

Proteins are entirely different than glycopeptide antibiotics such as dalbavancin. Different factors must be considered in the formulation of proteins.[1]

> Many sugars, polyols and amino acids protect from inactivation during freeze-drying. These excipients are preferentially excluded from the surface of proteins, and stabilize them thermodynamically against heat-denaturation and cold-denaturation. Molecular interactions, such as hydrogen bonding, between proteins and excipients are reported to be necessary for stabilization during the drying process.[2]

In contrast, the conventional wisdom for glycopeptide antibiotics is that no stabilizers are needed. For instance, vancomycin is one of most common comparators for the standard of care. (See specification, paragraphs [0006] and [0108]). As seen in the attached Material Safety Data Sheet for Vancomycin Hycrochloride for Injection (attached as Exhibit D), vancomycin does not contain any stabilizers (see Section 2) and yet is stable at normal temperatures and pressures (see Section 10). Similarly, daptomycin, another glycopeptide antibiotic used for the treatment of complicated skin and skin structure infections, does not have any stabilizers in the formulation.

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[1] *See, e.g.,* IZUTSU, K. et al. "Decreased Protein-Stabilizing Effects of Cryoprotectants Due to Crystallization" PHARMACEUTICAL RESEARCH 10(8): 1232-37, 1232 (1993) (Attached as Exhibit B)

> "The use of biotechnology has resulted in the production of proteins for pharmaceutical purposes. However, proteins are chemically and physically unstable, which causes problems during their purification, formulation and storage. Freeze-drying is often used for protein formulations to achieve long-term stability. Although the shelf lives may be improved by freeze-drying, some proteins are inactivated during this process. Additives, including sugars, amino acids, and surfactants, have been used to prevent inactivation during freeze-drying."

[2] IZUTSU, K. et al. "Effect of Mannitol Crystallinity on the Stabilization of Enzymes during Freeze-Drying." CHEM. PHARM. BULL. 42(1): 5-8, 5 (1994). (Attached as Exhibit C)

As described in the attached "Full Prescribing Information" description found at http://www.cubicin.com/documents/cubicin_compact_pi.pdf (attached as Exhibit E), "Cubicin is supplied as a sterile, preservative-free, pale yellow to light brown, lyophilized cake containing approximately 900 mg/g of daptomycin for intravenous use following reconstitution with 0.9% sodium chloride injection. The only inactive ingredient is sodium hydroxide, which is used in minimal quantities for pH adjustment." (see "Description," Col. 1) Contrary to this conventional wisdom, applicants have unexpectedly discovered a dramatic increase in the long-term stability of dalbavancin by adding a stabilizer. The prior art for other glycopeptide antibiotics therefore teaches away from the claimed invention.

Therefore, claim 1 is patentably distinct from the cited art. Claims 2-11 are dependent on claim 1 and are therefore patentably distinct from the cited art for the same reasons as applicable to claim 1. The rejections based on prior art should therefore be withdrawn.

CONCLUSION

For all the foregoing reasons, applicants assert that the claims are in condition for allowance. Favorable action on the merits of the claims is therefore earnestly solicited. If any issues remain, please contact the applicants' undersigned representative at (949) 737-2900. The Commissioner is hereby authorized to charge any fees that may be required in connection with the filing of these documents to Deposit Account No. 50-2862.

Respectfully submitted,

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